

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (Currently Amended) A method of promoting remyelination of nerve cells in a mammal comprising chronically administering to the mammal in need thereof a remyelinating agent in a remyelinating effective amount, wherein the remyelinating agent is an antibody or an immunologically active fragment thereof that binds to alpha-4 beta-1 integrin, and wherein the chronic administration of the remyelinating agent is weekly or monthly over a period of at least six months.
2. (Original) The method of claim 1, wherein the mammal is a human.
3. (Currently Amended) The method of claim 2, wherein the human suffers from a condition which demyelinates cells, and wherein the said condition is multiple sclerosis, a congenital metabolic disorder, a neuropathy with abnormal myelination, drug induced demyelination, radiation induced demyelination, a hereditary demyelinating condition, a prion induced demyelinating condition, encephalitis induced demyelination, or a spinal cord injury.
4. (Original) The method of claim 3, wherein the human suffers from multiple sclerosis.
5. (Canceled).
6. (Currently Amended) The method of claim ~~[[5]]~~ 1, wherein the antibody is a monoclonal antibody or an immunologically active fragment ~~of a monoclonal antibody thereof.~~

7. (Currently Amended) The method of claim 6, wherein the monoclonal antibody is a chimeric antibody, a human antibody, a genetically engineered antibody, [[or]] a bispecific antibody, or an immunologically active fragment thereof.

8. (Currently Amended) The method of claim 7, wherein the chimeric antibody is a humanized antibody, [[or]] a primatized antibody, or an immunologically active fragment thereof.

9. (Canceled).

10. (Currently Amended) The method of claim [[9]] 8, wherein the antibody is a humanized antibody or an immunologically active fragment thereof.

11. (Currently Amended) The method of claim [[8]] 10, wherein the humanized antibody is natalizumab or an immunologically active fragment thereof.

12. (Currently Amended) The method of claim [[ii]] 11, wherein natalizumab or an immunologically active fragment thereof is administered intravenously or subcutaneously.

13. (Currently Amended) The method of ~~any one of claims 5-11~~ claim 6, wherein the immunologically active fragment of the monoclonal antibody is an Fab, scFv, or F(ab')₂.

14. (Canceled).

15. (Currently Amended) The method of claim 12, wherein natalizumab or an immunologically active fragment thereof is administered intravenously to a mammal, and wherein the administration results in an effective blood level of natalizumab or an immunologically active fragment thereof in said mammal of at least about 1 ng/mL.

16. (Currently Amended) The method of claim 15, wherein the effective blood level of natalizumab or an immunologically active fragment thereof is about 4 ~~ng/ml~~ 10 ng/ml or more.

17. (Canceled).

18. (Currently Amended) The method of ~~claim 17~~ claim 1, wherein the chronic administration of the remyelinating agent is weekly or monthly over a period of at least one year.

19. (Original) The method of any one of claims 1-4, wherein an anti-inflammatory agent is co-administered with the remyelinating agent to the mammal.

20. (Original) The method of claim 19, wherein the anti-inflammatory agent is adrenocorticotrophic hormone, a corticosteroid, an interferon, glatiramer acetate, or a non-steroidal anti-inflammatory drug.

21. (Original) The method of claim 20, wherein the interferon is interferon beta-1b or interferon beta-1a.

22. (Currently Amended) The method of claim 20, wherein the corticosteroid is prednisone, methylprednisolone, dexamethasone, cortisol, cortisone, fludrocortisone, prednisolone, ~~6 α -methylprednisolone~~ 6 α -methylprednisolone, triamcinolone, or betamethasone.

23. (Original) The method of claim 22, wherein the corticosteroid is prednisone.

24. (Original) The method of claim 20, wherein the non-steroidal anti-inflammatory drug is aspirin, a sodium salicylate, choline magnesium trisalicylate, salsalate, diflunisal, sulfasalazine, olsalazine, a para-aminophenol derivatives, an indole, an indene acetic acid, a heteroaryl acetic acid, an anthranilic acid, an enolic

acid, an alkanones, a diaryl-substituted furanone, a diaryl-substituted pyrazoles, an indole acetic acids, or a sulfonanilide.

25. (Withdrawn) A combination therapy comprising a therapeutically effective amount of a remyelinating agent, which prevents demyelination and promotes remyelination when administered to a subject in need thereof, and an anti-inflammatory agent.

26. (Withdrawn) The combination therapy of claim 25, wherein the subject in need of remyelination suffers from multiple sclerosis, a congenital metabolic disorder, a neuropathy with abnormal myelination, drug induced demyelination, radiation induced demyelination, a hereditary demyelinating condition, a prion induced demyelinating condition, encephalitis induced demyelination, or a spinal cord injury.

27. (Withdrawn) The combination therapy of claim 25, wherein the remyelinating agent is an antibody or an immunologically active fragment thereof, wherein said antibody binds to VLA-4.

28. (Withdrawn) The combination therapy of claim 27, wherein the agent is an antibody that binds to alpha-4 beta-1 integrin.

29. (Withdrawn) The combination therapy of claim 25, wherein the remyelinating agent is an antibody or an immunologically active fragment thereof which binds to alpha-4 beta-1 integrin, and wherein the remyelinating agent is administered chronically to a patient in need thereof.

30. (Withdrawn) The combination therapy of claim 25, wherein the combination therapy comprises a therapeutically effective amount of a second remyelinating agent, which prevents demyelination and promotes remyelination when administered to a subject in need thereof, and wherein the first remyelinating

agent is a monoclonal antibody or an immunologically active fragment of a monoclonal antibody.

31. (Withdrawn) The combination therapy of claim 27, wherein the antibody is a monoclonal antibody.

32. (Withdrawn) The combination therapy of any of claims 30 or 31, wherein the monoclonal antibody is a chimeric antibody, a human antibody, a genetically engineered antibody, or a bispecific antibody.

33. (Withdrawn) The combination therapy of claim 32, wherein the chimeric antibody is humanized or primatized.

34. (Withdrawn) The combination therapy of claim 33, wherein the humanized antibody is natalizumab or an immunologically active fragment thereof.

35. (Withdrawn) The combination therapy of claim 30, wherein the second remyelinating agent is a compound of formula I, IA, IB, IC, II, II, or IIB.

36. (Withdrawn) The combination therapy of claim 35, wherein the second remyelinating agent is a compound of formula IB, IC, or IIB.

37. (Withdrawn) The combination therapy of claim 36, wherein the second remyelinating agent is *N*-[*N*-(3-pyridinesulfonyl)-L-3 ,3-dimethyl-4-thiaprolyl]-O-[1-methylpiperazin-4-ylcarbonyl]-L-tyrosine isopropyl ester.

38. (Withdrawn) The combination therapy of claim 25, wherein the anti-inflammatory agent is adrenocorticotrophic hormone, a corticosteroid, an interferon, glatiramer acetate, or a non-steroidal anti-inflammatory drug.

39. (Withdrawn) The combination therapy of claim 38, wherein the interferon is interferon beta-1b or interferon beta-1a.

40. (Withdrawn and Currently Amended) The combination therapy of claim 38, wherein the corticosteroid is prednisone, methylprednisolone, dexamethasone, cortisol, cortisone, fludrocortisone, prednisolone, ~~6 α -methylprednisolone~~ 6 α -methylprednisolone, triamcinolone, or betamethasone.

41. (Withdrawn) The combination therapy of claim 38, wherein the non-steroidal anti-inflammatory drug is aspirin, a sodium salicylate, choline magnesium trisalicylate, salsalate, diflunisal, sulfasalazine, olsalazine, a para-aminophenol derivatives, an indole, an indene acetic acid, a heteroaryl acetic acid, an anthranilic acid, an enolic acid, an alkanones, a diaryl-substituted furanone, a diaryl-substituted pyrazoles, an indole acetic acids, or a sulfonanilide.

42. (Withdrawn) The combination therapy of claim 38, wherein the non-steroidal anti-inflammatory drug is aspirin, a sodium salicylate, choline magnesium trisalicylate, salsalate, diflunisal, sulfasalazine, olsalazine, a para-aminophenol derivatives, an indole, an indene acetic acid, a heteroaryl acetic acid, an anthranilic acid, an enolic acid, an alkanones, a diaryl-substituted furanone, a diaryl-substituted pyrazoles, an indole acetic acids, or a sulfonanilide.

43. (Withdrawn) The combination therapy of claim 25, wherein the remyelinating agent is in a form for intravenous or subcutaneous administration.

44. (Withdrawn) The combination therapy of claim 25, wherein the remyelinating agent is administered chronically.

45. (Withdrawn) The combination therapy of claim 44, wherein the remyelinating agent is administered weekly or monthly for a period of at least a year to the patient in need thereof.

46. (Currently Amended) A method of reversing paralysis in a subject with a demyelinating disease comprising chronically administering to the subject a

remyelinating agent in an amount sufficient to inhibit lymphocyte infiltration of immune cells in the spinal cord to promote remyelination of nerve cells in the spinal cord and thereby treating paralysis in said subject in need thereof, wherein the myelinating agent is an antibody or an immunologically active fragment thereof that binds to alpha-4 beta-1 integrin, and wherein the chronic administration of the myelinating agent is weekly or monthly over a period of at least six months.

47. (Original) The method of claim 46, wherein the subject with paralysis suffers from multiple sclerosis, a congenital metabolic disorder, a neuropathy with abnormal myelination, drug induced demyelination, radiation induced demyelination, a hereditary demyelinating condition, a prion induced demyelinating condition, encephalitis induced demyelination, or a spinal cord injury.

48. (Original) The method of claim 46, wherein the subject is human.

49. (Original) The method of claim 46 further comprising co-administering an immunosuppressant.

50-51. (Canceled).

52. (Currently Amended) The method of claim [51]] 46, wherein the antibody is a monoclonal antibody or an immunologically active fragment thereof.

53. (Currently Amended) The method of claim 52, wherein the monoclonal antibody is a chimeric antibody, a human antibody, a genetically engineered antibody, [[or]] a bispecific antibody, or an immunologically active fragment thereof.

54. (Currently Amended) The method of claim 53, wherein the chimeric antibody is a humanized antibody, [[or]] a primatized antibody, or an immunologically active fragment thereof.

55. (Currently Amended) The method of claim 54, wherein the humanized antibody is natalizumab or an immunologically active fragment thereof.

56. (Currently Amended) The method of claim ~~[[51]]~~ 46, wherein the chronic administration of the remyelinating agent anti-VLA-4 antibody is administered weekly or monthly over a period of ~~for~~ at least one year.

57. (Original) The method of claim 49, wherein the immunosuppressant is adrenocorticotrophic hormone, a corticosteroid, or an interferon.

58. (Original) The method of claim 57, wherein the interferon is interferon beta-1b or interferon beta-1a.

59. (Currently Amended) The method of claim 57, wherein the corticosteroid is prednisone, methylprednisolone, dexamethasone, cortisol, cortisone, fludrocortisone, prednisolone, ~~6 α -methylprednisolone~~ 6 α -methylprednisolone, triamcinolone, or betamethasone.